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95% confidence limit for that rate ratio estimate as meaning that “a rate ratio as large as 4.2 has not been plausibly excluded” incorrectly implies that rate ratio values greater than 4.2 have been “plausibly excluded” (6).

Finally, the authors recommend “interpreting the variability around an effect estimate when making conclusions about causal associations,” implying that results of a single study can be conclusive regarding causality, but this can hardly ever happen, especially in an observational study. Thus, “making conclusions about causal associations” by any given study’s author(s) should be proscribed (and accordingly, the Conclusion(s) section in articles in medical journals should be abolished).

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Reply: More on Causal Inference Studies

From the Authors:

We thank Dr. Karp for highlighting the literature distinguishing etiologic and intervention conceptual approaches to the study of causation. Emulating a clinical trial in the design of observational studies, however, remains a powerful tool to understand causation. We disagree that this recommendation is a “failure.”

In writing for a clinical journal, we aimed to maximize comprehension at the expense of specificity on a few occasions (1). For example, we chose to use the term “casual association” to convey the idea that the associations we are interested in are causal in nature—that a causal model must underlie one’s thinking. Although it is not in common usage, authors may wish to use this term to describe the purpose of their study. We agree that it should not be used to justify claims of causality. We also used the word “confounding” to describe the effect of conditioning on a collider. Although this is not technically accurate, we conveyed the correct message.

The confidence interval is a measure of the precision of an estimate or measure. Imprecision is a reasonable term when confidence intervals are large. Confidence intervals that include the null value too often lead to claims of “no association,” even when they contain clinically or biologically meaningful effect sizes. This is particularly true when the point estimate is meaningfully large. We encourage authors to thoughtfully interpret effect estimates and confidence intervals rather than adhering to an alpha “litmus test” of 0.05.

A few of the points made in Dr. Karp’s letter suggest that we are implying something we are not. We do not state that a single

References

- 1 @yudapearl. This is an incredible vote of confidence in the methodology of #causal inference, especially in observational studies. The standards that regulate scientific writing shape scientific thoughts and practice. I wish editors of economics journals generate similar guidelines. #Bookofwhy. [posted 2019 Jan 5]. Available from: <https://twitter.com/yudapearl/status/1081799889267286016>.
- 2 Lederer DJ, Bell SC, Branson RD, Chalmers JD, Marshall R, Maslove DM, *et al*. Control of confounding and reporting of results in causal inference studies: guidance for authors from editors of respiratory, sleep, and critical care journals. *Ann Am Thorac Soc* 2019;16:22–28.
- 3 Karp I, Miettinen OS. On the essentials of etiological research for preventive medicine. *Eur J Epidemiol* 2014;29:455–457.
- 4 Kent DM, Steyerberg E, van Klaveren D. Personalized evidence based medicine: predictive approaches to heterogeneous treatment effects. *BMJ* 2018;363:k4245.
- 5 Karp I, Sylvestre MP, Abrahamowicz M, Leffondré K, Siemiatycki J. Bridging the etiologic and prognostic outlooks in individualized assessment of absolute risk of an illness: application in lung cancer. *Eur J Epidemiol* 2016;31:1091–1099.
- 6 Poole C. Confidence intervals exclude nothing. *Am J Public Health* 1987;77:492–493.

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study can prove causality, or that confidence intervals exclude effects outside of their boundaries, or that causal factors should be ignored in prediction models. Indeed, an important point of the paper was to instruct authors not to read things into their data that aren’t there. Equally, we encourage readers not to read things into our recommendations that weren’t there.

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[†]D.J.L. is Editor-in-Chief of *AnnalsATS*. His participation complies with American Thoracic Society requirements for recusal from review and decisions for authored works.

Reference

- 1 Lederer DJ, Bell SC, Branson RD, Chalmers JD, Marshall R, Maslove DM, *et al*. Control of confounding and reporting of results in causal inference studies. Guidance for authors from editors of respiratory, sleep, and critical care journals. *Ann Am Thorac Soc* 2019;16:22–28.

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